HED DOC. NO. 013764

September 29, 1999

MEMORANDUM

SUBJECT: ***ACIFLUORFEN*** - Report of the FQPA Safety Factor Committee.

FROM: Brenda Tarplee, Executive Secretary
FQPA Safety Factor Committee
Health Effects Division (7509C)

THROUGH: Ed Zager, Chair
FQPA Safety Factor Committee
Health Effects Division (7509C)

TO: Virginia Dobozy, Risk Assessor
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Health Effects Division (7509C)

PC Code: 114402

The Health Effects Division (HED) FQPA Safety Factor Committee met on September 13, 1999 to evaluate the hazard and exposure data for acifluorfen and recommended that the FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) be retained at 10x when assessing acute dietary and short-/intermediate-term residential (non-occupational) exposures and reduced to 3x when assessing chronic dietary and long-term residential (non-occupational) exposures

resulting from the use of this pesticide.

I. HAZARD ASSESSMENT

(*Memorandum:* P. Chin to V. Dobozy dated April 7, 1999)

1. Adequacy of Toxicity Database

The toxicology database for acifluorfen is adequate according to the Subdivision F Guideline requirements for a food-use chemical. However, the HIARC concluded that a developmental neurotoxicity study in rats is required for acifluorfen due to concern for the neurotoxic effects observed in the developing fetus (increase in anatomical variations including dilated lateral ventricles of the brain) in the prenatal developmental study in rats.

2. Determination of Susceptibility

The data provided no indication of increased susceptibility of rabbits following *in utero* exposure to acifluorfen or of rats following pre-/postnatal exposure. In the prenatal developmental toxicity study in rabbits, no evidence of developmental toxicity was seen even in the presence of maternal toxicity at the highest dose tested. And in the two-generation reproduction study in rats, effects in the offspring were observed only at or above treatment levels which resulted in evidence of parental toxicity.

However, qualitative evidence of increased susceptibility was found following *in utero* exposure to acifluorfen in the prenatal developmental toxicity study in rats. In this study, the developmental toxicity (decreased fetal body weight and increase in anatomical variations including dilated lateral ventricles of the brain) was seen in the presence of minimal maternal toxicity (clinical signs including excessive salivation and piloerection) at the same dose.

II. EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

1. Dietary (Food) Exposure Considerations

(*Correspondence:* W. Hazel to B. Tarplee dated Sept. 9, 1999)

Tolerances are established for combined residues of the herbicide sodium salt of acifluorfen and its metabolites (the corresponding acid, the methyl ester, and the amino analogs) in or on many foods considered to be highly consumed by infants and children including: rice, peanuts, and soybeans; and milk and meat. Tolerance levels for these commodities range from 0.02 - 0.1 ppm (40 CFR 180.383). There are no established Codex MRLs for acifluorfen.

Residues of acifluorfen are systemic and, if present, will not be removed by routine preparation (e.g., washing, peeling, etc.). Trace residues of acifluorfen are expected to transfer to livestock products (tolerances are established at 0.02 ppm).

There are no monitoring data for acifluorfen, however adequate field trial data are available and indicate nondetectable residues for all registered crops. Although BEAD percent crop treated (%CT) data are not available, the registrant has provided %CT data from 1994-98 for acifluorfen.

The HED Dietary Exposure Evaluation Model (DEEM) is used to assess the risk from acute and chronic dietary exposure to acifluorfen residues in food. At the time of this meeting, these analyses were not complete. Since there are no monitoring data, it is expected that these analyses could be refined using ARs from field trial data and the available %CT data which would result in a more realistic depiction of acute and chronic dietary food exposure resulting from the use of acifluorfen.

2. Dietary (Drinking Water) Exposure Considerations
(*Correspondence:* J. Wolf to B. Tarplee dated Sept. 10, 1999)

The environmental fate database for acifluorfen is adequate for the characterization of drinking water exposure. The data indicate that acifluorfen is highly mobile and can be very persistent depending upon the environmental conditions.

Monitoring data are available for acifluorfen including a "targeted" small scale prospective ground-water monitoring study. This study was conducted in a vulnerable area using maximum use rates and reported the highest detections. The ground water modeling output correspond to these data. The other monitoring studies were not specifically conducted for acifluorfen.

The drinking water exposure assessment for acifluorfen used monitoring data and modeling output. The models used in this assessment were PRZM and EXAMS for Tier II surface water assessment and SCI-GROW for a Tier I ground water assessment.

3. Residential Exposure Considerations
(*Correspondence:* K. Joseph to B. Tarplee dated Sept. 10, 1999)

Acifluorfen has registered residential uses. It is marketed as a ready-to-use spray for post-emergence grass and weed control on mulch, ornamental and/or shade trees, ornamental herbaceous plants, ornamental lawns and turf, ornamental woody shrubs and vines, paths/patios, and paved areas (private roads/sidewalks).

Since there are no chemical-specific data for post-application exposure resulting from the use of acifluorfen in non-occupational settings, the *Draft Standard Operating Procedures for Residential Exposure Assessments* will be used as the basis for all calculations. No deviations from SOPs are expected.

Based on the use pattern (spot treatments), minimal postapplication exposure is expected to infants and children from dermal contact or ingestion of acifluorfen in the residential environment.

III. SAFETY FACTOR RECOMMENDATION AND RATIONALE

1. FQPA Safety Factor Recommendation

The Committee recommended that the FQPA safety factor for protection of infants and children (as required by FQPA) should be retained at 10x when assessing acute dietary and short-/intermediate-term residential (non-occupational) exposures and reduced to 3x when assessing chronic dietary and long-term residential (non-occupational) exposures resulting from the use of acifluorfen.

2. Rationale for Requiring the FQPA Safety Factor

The FQPA SFC concluded that a safety factor is required because:

< there is qualitative evidence of increased susceptibility following *in utero* exposure to acifluorfen in the prenatal developmental toxicity study in rats (developmental toxicity was seen in the presence of minimal maternal toxicity at the same dose); and
< a developmental neurotoxicity study in rats is required for acifluorfen in order to further define the neurotoxic potential observed in the developing fetus in the prenatal developmental study in rats.

3. Application of the Safety Factor - Population Subgroups / Risk Assessment Scenarios

When assessing **Acute Dietary and Short-/Intermediate-term Residential (Non-occupational) Exposures,** the safety factor should be **Retained at 10x** for the **Females 13-50;** and the **Infants and Children Subgroups** since a qualitative increase in susceptibility was observed following *in utero* exposure to rats in the developmental study (which could potentially occur after a single dose); and since there is a datagap for the developmental neurotoxicity study in rats. The developmental neurotoxicity study is designed to evaluate neurotoxic effects on the mother and fetus from the time of implantation of the fertilized egg into the wall of the uterus through birth. This study may provide additional information which could be used to further characterize the effects of acifluorfen on the developing organism.

When assessing the **Chronic Dietary and Long-Term Residential Exposures,** the safety factor can be **Reduced to 3x** for the **Females 13-50;** and the **Infants and Children Subgroups** since there is a data gap for the developmental neurotoxicity study. (The qualitative increase in susceptibility seen after *in utero* exposure in the developmental study has no bearing on chronic exposure scenarios).